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EXAMINER

PONNALURI, PADMASHRI

ART UNIT

PAPER NUMBER

1639

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13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/904,186	Applicant(s) Pakula et al	
	Examiner Padmashri Ponnaluri	Art Unit 1639	
<i>-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --</i>			
Period for Reply A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION. <ul style="list-style-type: none"> - Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). - Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b). 			
Status <p>1) <input checked="" type="checkbox"/> Responsive to communication(s) filed on <u>Nov 25, 2002</u></p> <p>2a) <input type="checkbox"/> This action is FINAL. 2b) <input checked="" type="checkbox"/> This action is non-final.</p> <p>3) <input type="checkbox"/> Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i>, 1935 C.D. 11; 453 O.G. 213.</p>			
Disposition of Claims <p>4) <input checked="" type="checkbox"/> Claim(s) <u>1-65</u> is/are pending in the application.</p> <p>4a) Of the above, claim(s) <u>38-65</u> is/are withdrawn from consideration.</p> <p>5) <input type="checkbox"/> Claim(s) _____ is/are allowed.</p> <p>6) <input checked="" type="checkbox"/> Claim(s) <u>1-37</u> is/are rejected.</p> <p>7) <input type="checkbox"/> Claim(s) _____ is/are objected to.</p> <p>8) <input type="checkbox"/> Claims _____ are subject to restriction and/or election requirement.</p>			
Application Papers <p>9) <input type="checkbox"/> The specification is objected to by the Examiner.</p> <p>10) <input type="checkbox"/> The drawing(s) filed on _____ is/are a) <input type="checkbox"/> accepted or b) <input type="checkbox"/> objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).</p> <p>11) <input type="checkbox"/> The proposed drawing correction filed on _____ is: a) <input type="checkbox"/> approved b) <input type="checkbox"/> disapproved by the Examiner. If approved, corrected drawings are required in reply to this Office action.</p> <p>12) <input type="checkbox"/> The oath or declaration is objected to by the Examiner.</p>			
Priority under 35 U.S.C. §§ 119 and 120 <p>13) <input type="checkbox"/> Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).</p> <p>a) <input type="checkbox"/> All b) <input type="checkbox"/> Some* c) <input type="checkbox"/> None of: 1. <input type="checkbox"/> Certified copies of the priority documents have been received. 2. <input type="checkbox"/> Certified copies of the priority documents have been received in Application No. _____. 3. <input type="checkbox"/> Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).</p> <p>*See the attached detailed Office action for a list of the certified copies not received.</p> <p>14) <input type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e). a) <input type="checkbox"/> The translation of the foreign language provisional application has been received.</p> <p>15) <input checked="" type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.</p>			
Attachment(s) <p>1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)</p> <p>2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</p> <p>3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____</p> <p>4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____</p> <p>5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)</p> <p>6) <input type="checkbox"/> Other: _____</p>			

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DETAILED ACTION

1. This application is a continuation of application 08/978,381, filed on 11/25/97; which is a continuation of application 08/547,889, filed on 10/25/1995; which is a continuation-in-part of application 08/263,923, filed on 6/21/1994; which is a continuation in part of application 08/080,829, which is filed on 6/21/1993.

2. Applicant's election with traverse of group I, claims 1-37; and target bound to the solid phase as species of presence of target in Paper No. 8, filed on 7/9/02 is acknowledged. The traversal is on the ground(s) that group I and group II are not mutually exclusive, since group I methods are necessarily performed prior to group II inventions. This is not found persuasive because group II inventions, claims 38-44 which are drawn to the methods of screening for different properties. In group I methods the target protein which does not unfold in presence of the ligands are selected, which is different from the group II methods in which the selected ligands require further properties. Thus the ligands selected at the end of the group II methods and group I methods would not be the same. Further the method steps, and the assay conditions are different in group I compare to the group II methods. Thus, restriction between the groups is proper.

The requirement is still deemed proper and is therefore made FINAL.

3. Applicant's election with traverse of 'human neutrophil elastase enzyme as target protein; and MDL 101, 140 as species of the test ligand' in Paper No. 12, file don 11/25/02 is acknowledged. The traversal is on the ground(s) that the invention will detect any compound that binds to any sequence or domain. Applicants arguments have been fully considered and are not

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persuasive, since the instant claims recite very generic method claims, and the examiner has set forth the requirement as election of species, and not a restriction. And further the election of species is required for the purpose of search of the broad method claims. The claimed generic methods which are open to different ligands and targets which are related or specific to each other and the method steps require that prior to the assay method the information regarding the ligands and the target which bind to each other or do not bind to each other is required, thus the different species require an unduly extensive and burdensome search. And the species election for examination purpose is proper.

4. Claims 1-65 are currently pending in this application.

5. Claims 38-65 are withdrawn from further consideration pursuant to 37 CAR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Applicant timely traversed the restriction (election) requirement in Paper No.

6. Claims 1-37 are currently being examined din this application.

7. Claims 1-10, 13, 18-20, 23, 25-26, 29, 31-33, 36 may not have the benefit of the filing date of the parent application serial number 08/263,923, filed on 6/21/1994. The method for screening ‘more than 1000 compounds or excess of one thousand test ligands in a single day’ claimed in Claims 1-10, 13, 18-20, 23, 25-26, 29, 31-33, 36 has no clear support in parent application serial number 08/263,923.

If applicant disagrees, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the specification.

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8. The instant claims 1-10, 13, 18-20, 23, 25-26, 29, 31-33, 36 have effective filing date of parent application 08/547,889, filed on 10/25/1995.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites ‘a drug screening method’, however the instant claimed method steps do not show any correlation between the method steps and the drug. Does applicants ligand in the claimed method is ‘the drug’, it is not clear applicants are requested to amend the claim.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: the claimed method step g) recites selecting as a ligand for said target protein, however the instant method is drawn to a ‘a drug screening method’. The instant claimed method does not have any method steps in which drug or drugs are screened. Applicants are requested to amend the claim.

Claim 1 method recites in step a) ‘selecting as test ligands a plurality of compounds including those not known to bind to a target protein;’ and step b) recites ‘incubating one of said test ligands’ From the claim method step a) it is clear that prior to the claimed method

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ligands which are known to bind the target protein are selected. Thus, it is not clear what is the end result of the method steps, if ligand which are known to bind to the target are selected prior to the claimed method. Does applicants mean that the ligands which bind to the target or different from the ‘drug’ being selected. It is not clear. Applicants are requested to amend the claim.

Claim 1 method in step a) recites selecting as test ligands a plurality of compounds including those not known to bind to a target protein; and step b) recites ‘incubating **one of said test ligands and the target protein.....** and step c) recites incubating **the target protein in the absence of a test ligand...**’ The claimed method seems to be screening by incubating ‘one of said ligands’ with the target. However, the method step a) recites ‘selecting as test ligands plurality of compounds’, and it is not clear which one of the selected plurality of test ligands is incubated with the target step b). It is not clear how and/or which the test ligand is selected from the plurality of test ligands, and also the test ligands are already known to bind the target protein.

The method in claims 1-37 recite in step c) recites ‘incubating the target protein in the absence of a test ligand...’ It is not clear whether the test ligand in step b) is same as the test ligand in step c). Applicants are requested to amend the claims.

Claims 1-10, 13, 16-37 recites repeating steps a) through e) with more than thousand or a large number of test ligands., thus the claimed methods are interpreted as a single assay method which is repeated a number of times which is equal to the number of compounds being tested, it is not a single high throughput assay in which a plurality of compounds are tested in a single assay, i.e. screening of a library or an array of compounds.

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Claims 1-30 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the instant claims do not recite how the extent of the folded or unfolded state of the target protein in test combination and control combination are measured. Applicants are requested to amend the claim to include all the method steps.

Claim 2 recites ‘...by screening a plurality of test ligands for **ability to bind to a target protein**’, and step a) recites ‘selecting as test ligands **a plurality of compounds not known to bind to the target protein**’. Since prior to the claimed method plurality of test ligands which do not bind to the target protein are selected as in step a), thus it is not clear at the end of the claimed method which of the test ligands bind to the target protein are identified or selected..

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: the claimed method step g) recites selecting a lead compound, and the claimed method recites ‘.... by screening of test ligands for ability to bind to a target protein....’. It is not clear what is the relationship between the test ligands which bind to the target protein and the lead compound. Applicants are requested to amend the claim.

Claim 4 recites the limitation "said selected ligands". There is insufficient antecedent basis for this limitation in the claim or in claim 3.

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Claim 4 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: claimed method recites ‘.. Identifying at least one each of said selected ligands for possible development as a pharmaceutical.’ It is not clear what does applicants mean by ‘identifying at least one of the selected ligand as possible development as a pharmaceutical.’ The claimed method steps do not include how to identify from the selected ligands which would be pharmaceutical. Applicants are requested to amend the claim.

Claims 5, 25-30 are indefinite by reciting ‘small organic molecule’ in which the term ‘small’ is a relative term. It may be smaller compare to a bigger compound and has no metes and bounds. It is not clear what does applicant mean by small, and it is not clear relative to what the compounds are considered as small. Applicants are requested to amend the claim by reciting the size of the organic molecule.

Claim 16 recites ‘... identifying a ligand that binds to a predetermined target protein ...’, and step a) recites ‘selecting as test ligands a plurality of compounds not known to bind to the target protein’. Since prior to the claimed method plurality of test ligands which do not bind to the target protein are selected as in step a), thus it is not clear at the end of the claimed method which of the test ligands that bind to the target protein are identified.

Claims 18-24 recite that the conditions to cause the target protein in the control combination to unfoldcomprising heating said control combination...’ thus, the control combination and the test combination does not undergo the same method steps in the same

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reaction conditions. The independent claims recite ‘subjecting the test and control combinations to conditions sufficient to cause the target protein in the control combination to unfold..’, thus instant claims contradicts the method steps in the independent claims. And since the control combination has different conditions in which the target protein is unfolded, it is not clear how the comparison of the test combination and the control combination would result in selecting ligand. And the control combination is subjected to different conditions compared to the test combination it is not clear how it is considered as control combination. Applicants are requested to clarify.

Claims 31-37 are indefinite by reciting ‘...measuring the extent to which the target protein is unfolded in each of the test and control combination using **fluorescence spectroscopy**.’ however the instant claimed methods no where teaches a use of a fluorescence probe or tag such that the fluorescence of the compounds is measured.

Claims 31-37 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how the fluorescence spectroscopy is used to measure the folded or unfolded state of the target protein without the use of a fluorescence probe. Does applicants mean that either the target or test ligand are fluorescent and the fluorescence is dependent on the folded or unfolded state of the target protein. The specification does not disclose that the target being fluorescent in either folded state or unfolded state. Thus, applicants are requested to amend the claims to recite the method steps in which the fluorescence of the target protein is measured.

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11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. Claims 11-12, 14-17, 21-22, 24, 27-28, 30, 34-35 and 37 are rejected under 35 U.S.C. 102(a) as being anticipated by Volkin et al (Harnessing Biotechnology for the 21st century, pages 298-302, August 1992).

Volkin et al teach a binding assay in which a group or related and soluble, small organic compounds (relates to the plurality of test ligands of the instant claims) whose binding ability to the target protein FGF is not known, are incubated with the target protein and the extent of the protection from thermal induced unfolding is determined by either aggregation or changes of fluorescence. Volkin et al teach that the compounds which protect FGF (target protein) from unfolding have potential development as pharmaceuticals to stabilize FGF compositions. Volkin et al teach that the binding assay method is convenient technique to examine ligand interactions. Volkin et al teach fluorescence spectroscopy is a convenient method to monitor structural integrity of FGF. The reference clearly anticipates the claimed invention.

13. Claims 11-12, 14-17, 21-22, 24, 27-28, 30, 34-35 and 37 are rejected under 35 U.S.C. 102(a) as being anticipated by Tsai et al (pharmaceutical Research, vol. 10, May 1993, pages 649-659).

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Tsai et al teach a rapid screening procedure to identify compounds, including small organic compounds, which stabilize heat induced unfolding of a target protein. A plurality of compounds whose binding ability to the target protein FGF is not known, are incubated with the target protein and the amount or rate of thermal induced unfolding is determined by either aggregation or changes in fluorescence. Compounds that are promising, at least one, are then assayed for their effect on a bioactivity of the target protein. Tsai et al teach that the compounds are to be developed as part of pharmaceutical compositions for wound healing. The reference clearly anticipates the claimed invention.

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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15. Claims 1-10, 13, 18-20, 23, 25-26, 29, 31-33, 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Volkin et al (Harnessing Biotechnology for the 21st century, pages 298-302, August 1992) and Agrafiotis et al (US Patent 5,463,564). (NOTE that Agrafiotis et al filing date September 16, 1994 which is earlier than the effective filing date of the instant claims).

Volkin et al teach a binding assay in which a group or related and soluble, small organic compounds (relates to the plurality of test ligands of the instant claims) whose binding ability to the target protein FGF is not known, are incubated with the target protein and the extent of the protection from thermal induced unfolding is determined by either aggregation or changes of fluorescence. Volkin et al teach that the compounds which protect FGF (target protein) from unfolding have potential development as pharmaceuticals to stabilize FGF compositions. Volkin et al teach that the binding assay method is convenient technique to examine ligand interactions. Volkin et al teach fluorescence spectroscopy is a convenient method to monitor structural integrity of FGF.

The claimed invention differs from the prior art teachings by reciting ‘screening more than 1000 compounds per day’. Note that the recitation ‘more than 1000 compounds per day’ or rapid screening is not considered as patentably distinct from screening one compound. The limitation ‘more than 1000 compounds per day’ is dependent on the equipment and the automation methods used in the laboratory and is not patentably distinct from screening a single compound. However, Agrafiotis et al teach a system and method of automatically generating chemical compounds with desired properties. The reference teaches a diverse chemical library is robotically generated and

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analyzed. The reference teaches a computer based system and method for automatically generating chemical library and analyzing the chemical library robotically. The reference teaches that the chemical library is analyzed for fluorescence properties. The reference teaches that the library may contain 1000 to 5000 members and are screened or analyzed in a competitive binding assay. The reference teaches that using the system a plurality of structure activity models may be tested and evaluated in parallel. The reference teaches that the system can be adapted to generate chemical compounds having any useful properties that depend upon structure, composition or state. The reference teaches that the present invention enables the automatic and intelligent synthesis and screening of very large numbers of chemical compounds which would refer to high throughput screening or more than thousands compounds per day of the instant claims.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to screen more than one thousand compounds which would effect the folding and unfolding of the target compounds since Agrafiotis et al teach the use of the robotic methods in screening large number of compounds and Volkin et al teach the method of screening for compounds which would effect the folding and unfolding of the target compounds. A person skilled in the art would have been motivated to use the robotic methods taught by Agrafiotis et al with the methods taught by Volkin et al such that a large number of compounds are screened.

16. Claims 1-10, 13, 18-20, 23, 25-26, 29, 31-33, 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsai et al (Pharmaceutical Research, vol. 10, May 1993, pages 649-659)

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and Agrafiotis et al (US Patent 5,463,564). (NOTE that Agrafiotis et al filing date September 16, 1994 which is earlier than the effective filing date of the instant claims).

Tsai et al teach a rapid screening procedure to identify compounds, including small organic compounds, which stabilize heat induced unfolding of a target protein. A plurality of compounds whose binding ability to the target protein FGF is not known, are incubated with the target protein and the amount or rate of thermal induced unfolding is determined by either aggregation or changes in fluorescence. Compounds that are promising, at least one, are assayed for their effect on a bioactivity of the target protein. Tsai et al teach that the compounds are to be developed as part of pharmaceutical compositions for wound healing.

The claimed invention differs from the prior art teachings by reciting ‘screening more than 1000 compounds per day’. Note that the recitation ‘more than 1000 compounds per day’ or rapid screening is not considered as patentably distinct from screening one compound. The limitation ‘more than 1000 compounds per day’ is dependent on the equipment and the automation methods used in the laboratory and is not patentably distinct from screening a single compound. However, Agrafiotis et al teach a system and method of automatically generating chemical compounds with desired properties. The reference teaches a diverse chemical library is robotically generated and analyzed. The reference teaches a computer based system and method for automatically generating chemical library and analyzing the chemical library robotically. The reference teaches that the chemical library is analyzed for fluorescence properties. The reference teaches that the library may contain 1000 to 5000 members and are screened or analyzed in a competitive binding

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assay. The reference teaches that using the system a plurality of structure activity models may be tested and evaluated in parallel. The reference teaches that the system can be adapted to generate chemical compounds having any useful properties that depend upon structure, composition or state. The reference teaches that the present invention enables the automatic and intelligent synthesis and screening of very large numbers of chemical compounds which would refer to high throughput screening or more than thousands compounds per day of the instant claims.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to screen more than one thousand compounds which would effect the folding and unfolding of the target compounds since Agrafiotis et al teach the use of the robotic methods in screening large number of compounds and Tsai et al teach the method of screening for compounds which would effect the folding and unfolding of the target compounds. A person skilled in the art would have been motivated to use the robotic methods taught by Agrafiotis et al with the methods taught by Tsai et al such that a large number of compounds are screened in a single day.

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 U. S. P. Q. 645 (Fed. Cir. 1985); *In re Van Ornum*,

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686 F.2d 937, 214 U. S. P. Q. 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 U. S. P. Q. 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 U. S. P. Q. 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CAR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CAR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CAR 3.73(b).

18. Claims 1-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-47 of U.S. Patent No. 5,679,582. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims recite that more than 1000 compounds or test ligands are screened in a single day, which is not patentably distinct compare to the reference claimed method, since the reference teaches all the method steps.

19. Claims 1-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 5,585,277. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims recite that more than 1000 compounds or test ligands are screened in a single day, which is not patentably distinct compare to the reference claimed method, since the reference teaches a rapid and large scale screening method.

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20. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner is on ***Increased Flex Schedule*** and can normally be reached on Monday to Friday from 7.00 AM to 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri
Primary Examiner
Technology Center 1600
Art Unit 1639
19 February 2003



PADMASHRI PONNALURI
PRIMARY EXAMINER